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Application of: Himmelsbach et al.
International Application No.: PCT/EP00/01496
International Filing Date: 24 February 2000 (24.02.00)
Title: 4-AMINO-QUINAZOLINE AND QUINOLINE
DERIVATIVES HAVING AN INHIBITORY EFFECT
ON SIGNAL TRANSDUCTION MEDIATED BY
TYROSINE KINASES
Docket No.: 5/1252

Box PCT
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PRELIMINARY AMENDMENT

Sir:

Prior to commencing examination of the above-captioned application, please amend the application as set forth below.

AMENDMENTS

Please amend the application as set forth below. All references to page and line numbers relate to the published version of the international application, WO 00/51991.

In the Description

On page 1, after the title of the invention, insert the following new paragraph and headings:

--Related Applications

A' This application is derived from International Application No.
PCT/EP00/01496, filed February 24, 2000, pursuant to 35 USC §371.

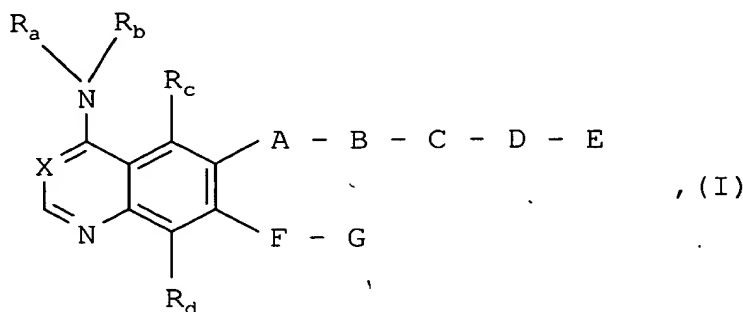
Description of the Invention--

On page 55, at line 11, delete the line of text which reads as follows:

“particularly the compounds characterized in claims 5 to 17,”

On page 55, after line 13, which reads “the tautomers, the stereoisomers and the salts thereof.”, add the new paragraphs that appear on the following pages.

Subgeneric aspect (5) of the invention is bicyclic heterocycles of general formula



wherein

R_a denotes a hydrogen atom or a C₁₋₄-alkyl group,

R_b denotes a phenyl, benzyl or 1-phenylethyl group wherein the phenyl nucleus is substituted in each case by the groups R₁ to R₃, whilst

R₁ and R₂, which may be identical or different, in each case denote a hydrogen, fluorine, chlorine, bromine or iodine atom,

a C₁₋₄-alkyl, hydroxy, C₁₋₄-alkoxy, C₃₋₆-cycloalkyl, C₄₋₆-cycloalkoxy, C₂₋₅-alkenyl or C₂₋₅-alkynyl group,

an aryl, aryloxy, arylmethyl or arylmethoxy group,

a C₃₋₅-alkenyloxy or C₃₋₅-alkynyloxy group, wherein the unsaturated moiety may not be linked to the oxygen atom,

a C₁₋₄-alkylsulphenyl, C₁₋₄-alkylsulphinyl, C₁₋₄-alkylsulphonyl, C₁₋₄-alkylsulphonyloxy, trifluoromethylsulphenyl, trifluoromethylsulphinyl or trifluoromethylsulphonyl group,

a methyl or methoxy group substituted by 1 to 3 fluorine atoms,

an ethyl or ethoxy group substituted by 1 to 5 fluorine atoms,

a cyano or nitro group or an amino group optionally substituted by one or two C₁₋₄-alkyl groups, wherein the substituents may be identical or different, or

R₁ together with R₂, if they are bound to adjacent carbon atoms, denote a -CH=CH-CH=CH-, -CH=CH-NH or -CH=N-NH group and

R₃ denotes a hydrogen, fluorine, chlorine or bromine atom,

a C₁₋₄-alkyl, trifluoromethyl or C₁₋₄-alkoxy group,

✓ R_c and R_d, which may be identical or different, in each case denote a hydrogen, fluorine or chlorine atom, a methoxy group, or a methyl group optionally substituted by a methoxy, dimethylamino, diethylamino, pyrrolidino, piperidino or morpholino group,

✓ X denotes a methine group substituted by a cyano group or a nitrogen atom,

✓ A denotes an oxygen atom or an imino group optionally substituted by a C₁₋₄-alkyl group,

✓ B denotes a carbonyl or sulphonyl group,

✓ C denotes a 1,3-allenylene, 1,1 or 1,2-vinylene group which may be substituted in each case by one or two methyl groups or by a trifluoromethyl group,

✓ an ethynylene group or

A₂ ✓ a 1,3-butadien-1,4-ylene group optionally substituted by 1 to 4 methyl groups or by a trifluoromethyl group,

✓ D denotes an alkylene, -CO-alkylene or -SO₂-alkylene group wherein the alkylene moiety in each case contains 1 to 8 carbon atoms and additionally 1 to 4 hydrogen atoms in the alkylene moiety may be replaced by fluorine atoms, whilst the linking of the -CO-alkylene and -SO₂-alkylene group to the adjacent group C in each case must take place via the carbonyl or sulphonyl group,

✓ a -CO-O-alkylene, -CO-NR₄-alkylene or -SO₂-NR₄-alkylene group wherein the alkylene moiety in each case contains 1 to 8 carbon atoms, whilst the linking to the adjacent group C in each case must take place via the carbonyl or sulphonyl group wherein

R₄ denotes a hydrogen atom or a C₁₋₄-alkyl group,

✓ or, if D is bound to a carbon atom of the group E, it may also denote a bond

✓ or, if D is bound to a nitrogen atom of the group E, it may also denote a carbonyl or sulphonyl group,

✓ E denotes an R₆O-CO-alkylene-NR₅, (R₇O-PO-OR₈)-alkylene-NR₅ or (R₇O-PO-R₉)-alkylene-NR₅-group wherein in each case the alkylene moiety, which is straight-chained and contains 1 to 6 carbon atoms, may additionally be substituted by one or two C₁₋₂-alkyl groups or by an R₆O-CO or R₆O-CO-C₁₋₂-alkyl group, wherein

R₅ denotes a hydrogen atom,

a C₁₋₄-alkyl group, which may be substituted by an R₆O-CO, (R₇O-PO-OR₈) or (R₇O-PO-R₉) group, /

an ethyl or propyl group optionally substituted by one or two methyl or ethyl groups, which may be terminally substituted in each case by a C₁₋₆-alkylcarbonylsulphenyl, C₃₋₇-cycloalkylcarbonylsulphenyl, C₃₋₇-cycloalkyl-C₁₋₃-alkylcarbonylsulphenyl, arylcarbonylsulphenyl or aryl-C₁₋₃-alkylcarbonylsulphenyl group,

an ethyl or propyl group optionally substituted by one or two methyl or ethyl groups which may be terminally substituted in each case by a C₁₋₆-alkylcarbonyloxy, C₃₋₇-cycloalkylcarbonyloxy, C₃₋₇-cycloalkyl-C₁₋₃-alkylcarbonyloxy, arylcarbonyloxy or aryl-C₁₋₃-alkylcarbonyloxy group,

A² an ethyl or propyl group optionally substituted by one or two methyl or ethyl groups, each of which may be terminally substituted by a hydroxy, C₁₋₄-alkoxy, amino, C₁₋₄-alkylamino or di-(C₁₋₄-alkyl)-amino group or by a 4- to 7-membered alkyleneimino group, whilst in the abovementioned 6- to 7-membered alkyleneimino groups a methylene group in the 4 position may be replaced by an oxygen or sulphur atom, by a sulphinyl, sulphonyl, imino or N-(C₁₋₄-alkyl)-imino group,

a C₃₋₇-cycloalkyl or C₃₋₇-cycloalkyl-C₁₋₃-alkyl group,

R₆, R₇ and R₈, which may be identical or different, in each case denote a hydrogen atom,

a C₁₋₈-alkyl group, which may be substituted by a hydroxy, C₁₋₄-alkoxy, amino, C₁₋₄-alkylamino or di-(C₁₋₄-alkyl)-amino group or by a 4- to 7-membered alkyleneimino group, whilst in the abovementioned 6- to 7-membered alkyleneimino groups in each case a methylene group in the 4 position may be replaced by an oxygen or sulphur atom or by a sulphinyl, sulphonyl, imino or N-(C₁₋₄-alkyl)-imino group,

a C₄₋₇-cycloalkyl group optionally substituted by 1 or 2 methyl groups,

a C₃₋₅-alkenyl or C₃₋₅-alkynyl group, wherein the unsaturated part may not be linked to the oxygen atom,

a C₃₋₇-cycloalkyl-C₁₋₄-alkyl, aryl, aryl-C₁₋₄-alkyl or R_gCO-O-(R_eCR_f)-group, whilst

R_e and R_f, which may be identical or different, in each case denote a hydrogen atom or a C₁₋₄-alkyl group and

✓ R_8 denotes a C_{1-4} -alkyl, C_{3-7} -cycloalkyl, C_{1-4} -alkoxy or C_{5-7} -cycloalkoxy group,

✓ and R_9 denotes a C_{1-4} -alkyl, aryl or aryl- C_{1-4} -alkyl group,

a 4- to 7-membered alkyleneimino group which may be substituted by an R_6O-CO , $(R_7O-PO-OR_8)$, $(R_7O-PO-R_9)$, $R_6O-CO-C_{1-4}$ -alkyl, bis- $(R_6O-CO)-C_{1-4}$ -alkyl, $(R_7O-PO-OR_8)-C_{1-4}$ -alkyl or $(R_7O-PO-R_9)-C_{1-4}$ -alkyl group wherein R_6 to R_9 are as hereinbefore defined,

a 4- to 7-membered alkyleneimino group which is substituted by two R_6OCO or R_6OCO-C_{1-4} -alkyl groups or by an R_6OCO -group and an R_6OCO-C_{1-4} -alkyl group wherein R_6 is as hereinbefore defined,

A² ✓ a piperazino or homopiperazino group which is substituted in the 4 position by the group R_{10} and is additionally substituted at a cyclic carbon atom by an R_6O-CO , $(R_7O-PO-OR_8)$, $(R_7O-PO-R_9)$, $R_6O-CO-C_{1-4}$ -alkyl, bis- $(R_6O-CO)-C_{1-4}$ -alkyl, $(R_7O-PO-OR_8)-C_{1-4}$ -alkyl or $(R_7O-PO-R_9)-C_{1-4}$ -alkyl group wherein R_6 to R_9 are as hereinbefore defined and

✓ R_{10} denotes a hydrogen atom, a C_{1-4} -alkyl, formyl, C_{1-4} -alkylcarbonyl or C_{1-4} -alkylsulphonyl group,

✓ a piperazino or homopiperazino group which is substituted in the 4 position by the group R_{10} and additionally at cyclic carbon atoms by two R_6O-CO or $R_6O-CO-C_{1-4}$ -alkyl groups or by an R_6O-CO -group and an $R_6O-CO-C_{1-4}$ -alkyl group wherein R_6 and R_{10} are as hereinbefore defined,

✓ a piperazino or homopiperazino group which is substituted in each case in the 4 position by an $R_6O-CO-C_{1-4}$ -alkyl, bis- $(R_6O-CO)-C_{1-4}$ -alkyl, $(R_7O-PO-OR_8)-C_{1-4}$ -alkyl or $(R_7O-PO-R_9)-C_{1-4}$ -alkyl group wherein R_6 to R_9 are as hereinbefore defined,

✓ a piperazino or homopiperazino group which is substituted in the 4 position by an $R_6O-CO-C_{1-4}$ -alkyl, bis- $(R_6O-CO)-C_{1-4}$ -alkyl, $(R_7O-PO-OR_8)-C_{1-4}$ -alkyl or $(R_7O-PO-R_9)-C_{1-4}$ -alkyl group and is additionally substituted at cyclic carbon atoms by one or two R_6O-CO or $R_6O-CO-C_{1-4}$ -alkyl groups or by an R_6O-CO -group and an $R_6O-CO-C_{1-4}$ -alkyl group wherein R_6 to R_9 are as hereinbefore defined,

✓ a morpholino or homomorpholino group which is substituted in each case by an R_6O-CO , $(R_7O-PO-OR_8)$, $(R_7O-PO-R_9)$, $R_6O-CO-C_{1-4}$ -alkyl, bis- $(R_6O-CO)-C_{1-4}$ -alkyl,

(R₇O-PO-OR₈)-C₁₋₄-alkyl or (R₇O-PO-R₉)-C₁₋₄-alkyl group wherein R₆ to R₉ are as hereinbefore defined,

a morpholino or homomorpholino group which is substituted by two R₆O-CO or R₆O-CO-C₁₋₄-alkyl groups or by an R₆O-CO-group and an R₆O-CO-C₁₋₄-alkyl group wherein R₆ is as hereinbefore defined,

a pyrrolidinyl, piperidinyl or hexahydroazepinyl group substituted in the 1 position by the group R₁₀, whilst the abovementioned 5- to 7-membered rings are additionally substituted in each case at a carbon atom by an R₆O-CO, (R₇O-PO-OR₈), (R₇O-PO-R₉), R₆O-CO-C₁₋₄-alkyl, bis-(R₆O-CO)-C₁₋₄-alkyl, (R₇O-PO-OR₈)-C₁₋₄-alkyl or (R₇O-PO-R₉)-C₁₋₄-alkyl group wherein R₆ to R₁₀ are as hereinbefore defined,

a pyrrolidinyl, piperidinyl or hexahydroazepinyl group substituted in the 1 position by the group R₁₀, while the abovementioned 5- to 7-membered rings are in each case additionally substituted at carbon atoms by two R₆O-CO or R₆O-CO-C₁₋₄-alkyl groups or by an R₆O-CO-group and an R₆O-CO-C₁₋₄-alkyl group wherein R₆ and R₁₀ are as hereinbefore defined,

a pyrrolidinyl, piperidinyl or hexahydroazepinyl group substituted in the 1 position by an R₆O-CO-C₁₋₄-alkyl, bis-(R₆O-CO)-C₁₋₄-alkyl, (R₇O-PO-OR₈)-C₁₋₄-alkyl or (R₇O-PO-R₉)-C₁₋₄-alkyl group wherein R₆ to R₉ are as hereinbefore defined,

a pyrrolidinyl, piperidinyl or hexahydroazepinyl group substituted in the 1 position by an R₆O-CO-C₁₋₄-alkyl, bis-(R₆O-CO)-C₁₋₄-alkyl, (R₇O-PO-OR₈)-C₁₋₄-alkyl or (R₇O-PO-R₉)-C₁₋₄-alkyl group, while the abovementioned 5- to 7-membered rings are in each case additionally substituted at carbon atoms by one or two R₆O-CO or R₆O-CO-C₁₋₄-alkyl groups or by an R₆O-CO-group and an R₆O-CO-C₁₋₄-alkyl group wherein R₆ to R₉ are as hereinbefore defined,

a 2-oxo-morpholino group which may be substituted by 1 to 4 C₁₋₂-alkyl groups,

a 2-oxo-thiomorpholino group which may be substituted by 1 to 4 C₁₋₂-alkyl groups,

a morpholino or thiomorpholino group which is substituted in the 2 position by a C₁₋₄-alkoxy group,

a morpholino or thiomorpholino group which is substituted in the 2 and 6 positions by a C₁₋₄-alkoxy group,

a C₁₋₄-alkyl-NR₅-group wherein the C₁₋₄-alkyl moiety, which is straight-chained and may additionally be substituted by one or two methyl groups, is in each case terminally substituted by a di-(C₁₋₄-alkoxy)-methyl or tri-(C₁₋₄-alkoxy)-methyl group, whilst R₅ is as hereinbefore defined,

a C₁₋₄-alkyl-NR₅-group wherein the C₁₋₄-alkyl moiety, which is straight-chained and may additionally be substituted by one or two methyl groups, is in each case terminally substituted by a 1,3-dioxolan-2-yl or 1,3-dioxan-2-yl group optionally substituted by one or two methyl groups, while R₅ is as hereinbefore defined,

an R₁₁NR₅-group wherein R₅ is as hereinbefore defined and

R₁₁ denotes a 2-oxo-tetrahydrofuran-3-yl, 2-oxo-tetrahydrofuran-4-yl, 2-oxo-tetrahydropyran-3-yl, 2-oxo-tetrahydropyran-4-yl, 2-oxo-tetrahydropyran-5-yl, 2-oxo-tetrahydrothiophen-3-yl, 2-oxo-tetrahydrothiophen-4-yl, 2-oxo-tetrahydrothiopyran-3-yl, 2-oxo-tetrahydrothiopyran-4-yl or 2-oxo-tetrahydrothiopyran-5-yl group optionally substituted by one or two methyl groups,

or D together with E denotes an R_gCO-O-(R_eCR_f)-O-CO, (R₇O-PO-OR₈) or (R₇O-PO-R₉)-group wherein R_e to R_g and R₇ to R₉ are as hereinbefore defined,

A² F and G together denote a hydrogen atom,

a C₁₋₆-alkoxy group optionally substituted from position 2 onwards by a hydroxy or C₁₋₄-alkoxy group,

a C₃₋₇-cycloalkoxy or C₃₋₇-cycloalkyl-C₁₋₄-alkoxy group,

whilst by the aryl moieties mentioned in the definitions of the abovementioned groups is meant a phenyl group which in each case may be monosubstituted by R₁₂, mono-, di- or trisubstituted by R₁₃ or monosubstituted by R₁₂ and additionally mono- or disubstituted by R₁₃, whilst the substituents may be identical or different and

R₁₂ denotes a cyano, carboxy, C₁₋₄-alkoxycarbonyl, aminocarbonyl, C₁₋₄-alkylaminocarbonyl, di-(C₁₋₄-alkyl)-aminocarbonyl, C₁₋₄-alkylsulphenyl, C₁₋₄-alkylsulphinyl, C₁₋₄-alkylsulphonyl, hydroxy, C₁₋₄-alkylsulphonyloxy, trifluoromethyloxy, nitro, amino, C₁₋₄-alkylamino, di-(C₁₋₄-alkyl)-amino, C₁₋₄-alkyl-carbonylamino, N-(C₁₋₄-alkyl)-C₁₋₄-alkylcarbonylamino, C₁₋₄-alkylsulphonylamino, N-(C₁₋₄-alkyl)-C₁₋₄-alkylsulphonylamino, aminosulphonyl, C₁₋₄-alkylaminosulphonyl or di-(C₁₋₄-alkyl)-aminosulphonyl group or a carbonyl group, which is substituted by a 5- to 7-membered alkyleneimino group, wherein in the abovementioned 6- to 7-membered alkyleneimino groups in each case a methylene group in the 4 position may be replaced by an oxygen or sulphur atom, by a sulphinyl, sulphonyl, imino or N-(C₁₋₄-alkyl)-imino-group, and

R₁₃ denotes a fluorine, chlorine, bromine or iodine atom, a C₁₋₄-alkyl, trifluoromethyl or C₁₋₄-alkoxy group or

two groups R₁₃, if they are bound to adjacent carbon atoms, together denote a C_{3,5}-alkylene, methylenedioxy or 1,3-butadien-1,4-ylene group,

the tautomers, the stereoisomers and the salts thereof.

Subgeneric aspect (6) of the invention is bicyclic heterocycles of general formula I, wherein

R_a denotes a hydrogen atom,

R_b denotes a phenyl, benzyl or 1-phenylethyl group wherein the phenyl nucleus is substituted in each case by the groups R_1 to R_3 , while

R_1 and R_2 , which may be identical or different, each denote a hydrogen, fluorine, chlorine, bromine or iodine atom,

a methyl, ethyl, hydroxy, methoxy, ethoxy, amino, cyano, vinyl or ethynyl group,

an aryl, aryloxy, arylmethyl or arylmethoxy group,

a methyl or methoxy group substituted by 1 to 3 fluorine atoms or

R_1 together with R_2 , if they are bound to adjacent carbon atoms, denote a $-\text{CH}=\text{CH}-\text{CH}=\text{CH}-$, $-\text{CH}=\text{CH}-\text{NH}$ or $-\text{CH}=\text{N}-\text{NH}$ group and

R_3 denotes a hydrogen, fluorine, chlorine or bromine atom,

R_c and R_d in each case denote a hydrogen atom,

X denotes a methine group substituted by a cyano group or a nitrogen atom,

A denotes an imino group optionally substituted by a methyl or ethyl group,

B denotes a carbonyl group,

C denotes a 1,1- or 1,2-vinylene group which is substituted in each case by one or two methyl groups or may be substituted by a trifluoromethyl group,

an ethynylene group or

a 1,3-butadien-1,4-ylene group optionally substituted by a methyl or trifluoromethyl group,

D denotes an alkylene or $-\text{CO}-$ alkylene group wherein the alkylene moiety in each case contains 1 to 4 carbon atoms, while the linking of the $-\text{CO}-$ alkylene group to the adjacent group C in each case must take place via the carbonyl group,

a $-\text{CO}-\text{O}-$ alkylene or $-\text{CO}-\text{NR}_4-$ alkylene- group wherein the alkylene moiety in each case contains 1 to 4 carbon atoms, while the linking to the adjacent group C in each case must take place via the carbonyl group wherein

R_4 denotes a hydrogen atom or a methyl or ethyl group,

or, if D is bound to a carbon atom of the group E, it may also denote a bond

or, if D is bound to a nitrogen atom of the group E, it may also denote a carbonyl or sulphonyl group,

E denotes an R_6O-CO -alkylene- NR_5 , $(R_7O-PO-OR_8)$ -alkylene- NR_5 or $(R_7O-PO-R_9)$ -alkylene- NR_5 group wherein in each case the alkylene moiety, which is straight-chained and contains 1 to 4 carbon atoms, may additionally be substituted by one or two C_{1-2} -alkyl groups or by an R_6O-CO or $R_6O-CO-C_{1-2}$ -alkyl group, while

R_5 denotes a hydrogen atom,

a C_{1-4} -alkyl group which may be substituted by an R_6O-CO group,

A² an ethyl or propyl group optionally substituted by one or two methyl or ethyl groups which is terminally substituted in each case by a hydroxy, C_{1-4} -alkoxy, di- $(C_{1-4}$ -alkyl)amino, C_{1-6} -alkylcarbonylsulphenyl, C_{3-6} -cycloalkylcarbonylsulphenyl, C_{3-6} -cycloalkyl- C_{1-3} -alkylcarbonylsulphenyl, arylcarbonylsulphenyl or aryl- C_{1-3} -alkylcarbonylsulphenyl group,

an ethyl or propyl group optionally substituted by one or two methyl or ethyl groups which is terminally substituted in each case by a C_{1-6} -alkylcarbonyloxy, C_{3-6} -cycloalkylcarbonyloxy, C_{3-6} -cycloalkyl- C_{1-3} -alkylcarbonyloxy, arylcarbonyloxy or aryl- C_{1-3} -alkylcarbonyloxy group,

a C_{3-6} -cycloalkyl or C_{3-6} -cycloalkyl- C_{1-3} -alkyl group,

R_6 , R_7 and R_8 , which may be identical or different, in each case denote a hydrogen atom,

a C_{1-8} -alkyl group which may be substituted by a hydroxy, C_{1-4} -alkoxy, or di- $(C_{1-4}$ -alkyl)-amino group or by a 4- to 7-membered alkyleneimino group, while in the abovementioned 6- to 7-membered alkyleneimino groups in each case a methylene group in the 4 position may be replaced by an oxygen atom or by an N- $(C_{1-2}$ -alkyl)-imino group,

a C_{4-6} -cycloalkyl group,

a C_{3-5} -alkenyl or C_{3-5} -alkynyl group, while the unsaturated moiety may not be linked to the oxygen atom,

a C_{3-6} -cycloalkyl- C_{1-4} -alkyl, aryl, aryl- C_{1-4} -alkyl or $R_gCO-O-(R_eCR_f)$ group, while

✓ R_e and R_f , which may be identical or different, in each case denote a hydrogen atom or a C_{1-4} -alkyl group and

✓ R_g denotes a C_{1-4} -alkyl, C_{3-6} -cycloalkyl, C_{1-4} -alkoxy or C_{5-6} -cycloalkoxy group,

✓ and R_9 denotes a C_{1-4} -alkyl group,

✓ a 4- to 7-membered alkyleneimino group which is substituted by an R_6O-CO , $R_6O-CO-C_{1-4}$ -alkyl or bis- $(R_6O-CO)-C_{1-4}$ -alkyl group wherein R_6 is as hereinbefore defined,

✓ a 4- to 7-membered alkyleneimino group which is substituted by two R_6O-CO or $R_6O-CO-C_{1-4}$ -alkyl groups wherein R_6 is as hereinbefore defined,

✓ a piperazino or homopiperazino group which is substituted in the 4 position by the group R_{10} and additionally at a cyclic carbon atom by an R_6O-CO , $R_6O-CO-C_{1-4}$ -alkyl or bis- $(R_6O-CO)-C_{1-4}$ -alkyl group wherein R_6 is as hereinbefore defined and

✓ R_{10} denotes a hydrogen atom, a methyl or ethyl group,

✓ a piperazino or homopiperazino group which is substituted in the 4 position by the group R_{10} and is additionally substituted at cyclic carbon atoms by two R_6O-CO or $R_6O-CO-C_{1-4}$ -alkyl groups wherein R_6 and R_{10} are as hereinbefore defined,

✓ a piperazino or homopiperazino group which is substituted in each case in the 4 position by an $R_6O-CO-C_{1-4}$ -alkyl, bis- $(R_6O-CO)-C_{1-4}$ -alkyl, $(R_7O-PO-OR_8)-C_{1-4}$ -alkyl or $(R_7O-PO-R_9)-C_{1-4}$ -alkyl group wherein R_6 to R_9 are as hereinbefore defined,

✓ a piperazino or homopiperazino group which is substituted in the 4 position by an $R_6O-CO-C_{1-4}$ -alkyl or bis- $(R_6O-CO)-C_{1-4}$ -alkyl group and is additionally substituted at cyclic carbon atoms by one or two R_6O-CO or $R_6O-CO-C_{1-4}$ -alkyl groups wherein R_6 is as hereinbefore defined,

✓ a morpholino or homomorpholino group which is substituted in each case by an R_6O-CO , $R_6O-CO-C_{1-4}$ -alkyl, or bis- $(R_6O-CO)-C_{1-4}$ -alkyl group wherein R_6 is as hereinbefore defined,

✓ a morpholino or homomorpholino group which is substituted by two R_6O-CO or $R_6O-CO-C_{1-4}$ -alkyl groups wherein R_6 is as hereinbefore defined,

a pyrrolidinyl, piperidinyl or hexahydroazepinyl group substituted in the 1 position by the group R_{10} , while the abovementioned 5- to 7-membered rings in each case are additionally substituted at a carbon atom by an R_6O-CO , $R_6O-CO-C_{1-4}$ -alkyl or bis- $(R_6O-CO)-C_{1-4}$ -alkyl group wherein R_6 and R_{10} are as hereinbefore defined,

a pyrrolidinyl, piperidinyl or hexahydroazepinyl group substituted in the 1 position by the group R_{10} , while the abovementioned 5- to 7-membered rings in each case are additionally substituted at carbon atoms by two R_6O-CO or $R_6O-CO-C_{1-4}$ -alkyl groups wherein R_6 and R_{10} are as hereinbefore defined,

a pyrrolidinyl, piperidinyl or hexahydroazepinyl group substituted in the 1 position by an $R_6O-CO-C_{1-4}$ -alkyl, bis- $(R_6O-CO)-C_{1-4}$ -alkyl, $(R_7O-PO-OR_8)-C_{1-4}$ -alkyl or $(R_7O-PO-R_9)-C_{1-4}$ -alkyl group wherein R_6 to R_9 are as hereinbefore defined,

A2 a pyrrolidinyl, piperidinyl or hexahydroazepinyl group substituted in the 1 position by an $R_6O-CO-C_{1-4}$ -alkyl or bis- $(R_6O-CO)-C_{1-4}$ -alkyl group, while the abovementioned 5- to 7-membered rings in each case are additionally substituted at carbon atoms by one or two R_6O-CO or $R_6O-CO-C_{1-4}$ -alkyl groups wherein R_6 is as hereinbefore defined,

a 2-oxo-morpholino group which may be substituted by 1 to 4 C_{1-2} -alkyl groups,

a 2-oxo-thiomorpholino group which may be substituted by 1 to 4 C_{1-2} -alkyl groups,

a morpholino group which is substituted in the 2 position by a C_{1-4} -alkoxy group,

a morpholino group which is substituted in the 2 and 6 positions in each case by a C_{1-4} -alkoxy group,

a C_{1-4} -alkyl- NR_5 group wherein the C_{1-4} -alkyl moiety, which is straight-chained, is terminally substituted by a di- $(C_{1-4}$ -alkoxy)-methyl group, while R_5 is as hereinbefore defined,

a C_{1-4} -alkyl- NR_5 group wherein the C_{1-4} -alkyl moiety, which is straight-chained, is terminally substituted by a 1,3-dioxolan-2-yl or 1,3-dioxan-2-yl group, while R_5 is as hereinbefore defined,

a $R_{11}NR_5$ group wherein R_5 is as hereinbefore defined and

R_{11} denotes a 2-oxo-tetrahydrofuran-3-yl, 2-oxo-tetrahydrofuran-4-yl, 2-oxo-tetrahydropyran-3-yl, 2-oxo-tetrahydropyran-4-yl, 2-oxo-tetrahydropyran-5-yl, 2-oxo-tetrahydrothiophen-3-yl, 2-oxo-tetrahydrothiophen-4-yl, 2-oxo-tetrahydrothiopyran-3-yl, 2-oxo-tetrahydrothiopyran-4-yl or 2-oxo-tetrahydrothiopyran-5-yl group optionally substituted by one or two methyl groups,

or D together with E denotes an $R_g\text{CO-O-(R}_e\text{CR}_f\text{)-O-CO}$ or $(R_7\text{O-PO-OR}_8)$ group wherein R_e to R_g and R_7 to R_9 are as hereinbefore defined,

F and G together denote a hydrogen atom,

a C_{1-6} -alkoxy group optionally substituted from position 2 by a hydroxy or C_{1-4} -alkoxy group,

a C_{4-7} -cycloalkoxy or C_{3-7} -cycloalkyl- C_{1-4} -alkoxy group,

whilst by the aryl moieties mentioned in the definitions of the abovementioned groups is meant a phenyl group which in each case may be monosubstituted by R_{12} , mono- or disubstituted by R_{13} or monosubstituted by R_{12} and additionally mono- or disubstituted by R_{13} , whilst the substituents may be identical or different and

R_{12} denotes a cyano, C_{1-2} -alkoxycarbonyl, aminocarbonyl, C_{1-2} -alkylaminocarbonyl, di- $(C_{1-2}$ -alkyl)-aminocarbonyl, C_{1-2} -alkylsulphenyl, C_{1-2} -alkylsulphinyl, C_{1-2} -alkylsulphonyl, hydroxy, nitro, amino, C_{1-2} -alkylamino or di- $(C_{1-2}$ -alkyl)-amino, and

R_{13} denotes a fluorine, chlorine, bromine or iodine atom, a C_{1-2} -alkyl, trifluoromethyl or C_{1-2} -alkoxy group or

two groups R_{13} , if they are bound to adjacent carbon atoms, together denote a C_{3-5} -alkylene, methylenedioxy or 1,3-butadien-1,4-ylene group,

the tautomers, the stereoisomers and the salts thereof.

Subgeneric aspect (7) of the invention is bicyclic heterocycles of general formula I, wherein

R_a denotes a hydrogen atom,

R_b denotes a phenyl, benzyl or 1-phenylethyl group wherein the phenyl nucleus is substituted in each case by the groups R_1 to R_3 , while

R_1 and R_2 , which may be identical or different, each denote a hydrogen, fluorine, chlorine or bromine atom, or a methyl, trifluoromethyl, methoxy, ethynyl or cyano group,

R_3 denotes a hydrogen atom,

R_c and R_d in each case denote a hydrogen atom,

X denotes a methine group substituted by a cyano group, or a nitrogen atom,

A denotes an imino group,

B denotes a carbonyl group,

C denotes a 1,1- or 1,2-vinylene group,

an ethynylene group or

a 1,3-butadien-1,4-ylene group,

D denotes a C₁₋₄-alkylene group,

a -CO-NR₄-alkylene group wherein the alkylene moiety contains 2 to 4 carbon atoms, while the linking to the adjacent group C in each case must take place via the carbonyl group, wherein

A² R₄ denotes a hydrogen atom,

or, if D is bound to a carbon atom of the group E, it may also denote a bond

or, if D is bound to a nitrogen atom of the group E, it may also denote a carbonyl group,

E denotes an R₆O-CO-alkylene-NR₅, (R₇O-PO-OR₈)-alkylene-NR₅ or (R₇O-PO-R₉)-alkylene-NR₅ group wherein in each case the alkylene moiety, which is straight-chained and contains 1 to 4 carbon atoms, may additionally be substituted by one or two C₁₋₂-alkyl groups or by an R₆O-CO or R₆O-CO-C₁₋₂-alkyl group, while

R₅ denotes a hydrogen atom,

a C₁₋₄-alkyl group which may be substituted by an R₆O-CO group,

an ethyl group optionally substituted by one or two methyl or ethyl groups which is terminally substituted by a C₁₋₄-alkylcarbonylsulphenyl, arylcarbonylsulphenyl or arylmethylcarbonylsulphenyl group,

an ethyl group optionally substituted by one or two methyl or ethyl groups which is terminally substituted by a hydroxy, C₁₋₄-alkylcarbonyloxy, arylcarbonyloxy or arylmethylcarbonyloxy group,

a 2,2-dimethoxyethyl or 2,2-diethoxyethyl group,

a C₃₋₆-cycloalkyl or C₃₋₆-cycloalkyl-methyl group,

R₆, R₇ and R₈, which may be identical or different, in each case denote a hydrogen atom,

a C₁₋₈-alkyl group,

a cyclopentyl, cyclopentylmethyl, cyclohexyl or cyclohexylmethyl group,

an aryl, arylmethyl or R_gCO-O-(R_eCR_f) group, wherein

R_e denotes a hydrogen atom or a C₁₋₄-alkyl group,

R_f denotes a hydrogen atom and

R_g denotes a C₁₋₄-alkyl, cyclopentyl, cyclohexyl, C₁₋₄-alkoxy, cyclopentyloxy or cyclohexyloxy group,

and R₉ denotes a methyl or ethyl group,

A² a pyrrolidino or piperidino group which is substituted by an R₆O-CO or R₆O-CO-C₁₋₂-alkyl group wherein R₆ is as hereinbefore defined,

a pyrrolidino or piperidino group which is substituted by two R₆O-CO or R₆O-CO-C₁₋₂-alkyl groups wherein R₆ is as hereinbefore defined,

a piperazino group which is substituted in the 4 position by the group R₁₀ and is additionally substituted at a cyclic carbon atom by an R₆O-CO or R₆O-CO-C₁₋₂-alkyl group, while R₆ is as hereinbefore defined and

R₁₀ denotes a hydrogen atom, a methyl or ethyl group,

a piperazino group which is substituted in the 4 position by an R₆O-CO-C₁₋₄-alkyl, bis-(R₆O-CO)-C₁₋₄-alkyl or (R₇O-PO-OR₈)-C₁₋₂-alkyl group wherein R₆ to R₈ are as hereinbefore defined,

a piperazino group which is substituted in the 4 position by an R₆O-CO-C₁₋₂-alkyl group and is additionally substituted at a cyclic carbon atom by an R₆O-CO or R₆O-CO-C₁₋₂-alkyl group wherein R₆ is as hereinbefore defined,

a morpholino group which is substituted by an R₆O-CO or R₆O-CO-C₁₋₂-alkyl group, while R₆ is as hereinbefore defined,

a piperidiny group substituted in the 1 position by an R₆O-CO-C₁₋₄-alkyl, bis-(R₆O-CO)-C₁₋₄-alkyl or (R₇O-PO-OR₈)-C₁₋₂-alkyl group wherein R₆ to R₈ are as hereinbefore defined,

a 2-oxo-morpholino group which may be substituted by 1 to 2 C₁₋₂-alkyl groups,

a 2-oxo-thiomorpholino group which may be substituted by 1 to 2 C₁₋₂-alkyl groups,

a morpholino group which is substituted in the 2 position by a methoxy or ethoxy group,

a morpholino group which is substituted in the 2 and 6 positions in each case by a methoxy or ethoxy group,

a 2,2-dimethoxyethyl-NR₅, 2,2-diethoxyethyl-NR₅, 1,3-dioxolan-2-yl-methyl-NR₅ or 1,3-dioxan-2-yl-methyl-NR₅ group wherein R₅ is as hereinbefore defined,

a N-methyl-R₁₁N or N-ethyl-R₁₁N group wherein

A² R₁₁ denotes a 2-oxo-tetrahydrofuran-3-yl, 2-oxo-tetrahydrofuran-4-yl, 2-oxo-tetrahydropyran-3-yl, 2-oxo-tetrahydropyran-4-yl, 2-oxo-tetrahydropyran-5-yl, 2-oxo-tetrahydrothiophen-3-yl, 2-oxo-tetrahydrothiophen-4-yl, 2-oxo-tetrahydrothiopyran-3-yl, 2-oxo-tetrahydrothiopyran-4-yl or 2-oxo-tetrahydrothiopyran-5-yl group optionally substituted by one or two methyl groups,

or D together with E denotes an R_gCO-O-(R_eCR_f)-O-CO or (R₇O-PO-OR₈) group wherein R_e to R_g and R₇ and R₈ are as hereinbefore defined,

F and G together denote a hydrogen atom, a methoxy, ethoxy, C₄₋₆-cycloalkoxy or C₃₋₆-cycloalkyl-C₁₋₃-alkoxy group,

while the aryl moieties mentioned in the definition of the abovementioned groups denote a phenyl group which may be mono- or disubstituted by R₁₃, while the substituents may be identical or different and

R₁₃ denotes a fluorine, chlorine, bromine or iodine atom, a C₁₋₂-alkyl, trifluoromethyl or C₁₋₂-alkoxy group or

two groups R₁₃, if they are bound to adjacent carbon atoms, together denote a C₃₋₄-alkylene, methylenedioxy or 1,3-butadien-1,4-ylene group,

the tautomers, the stereoisomers and the salts thereof.

Subgeneric aspect (8) of the invention is bicyclic heterocycles of general formula I, wherein

R_a denotes a hydrogen atom,

R_b denotes a phenyl, benzyl or 1-phenylethyl group wherein the phenyl nucleus is substituted in each case by the groups R₁ to R₃, wherein

R_1 and R_2 , which may be identical or different, each denote a hydrogen, fluorine, chlorine or bromine atom or a methyl group and

R_3 denotes a hydrogen atom,

R_c and R_d each denote a hydrogen atom,

X denotes a methine group substituted by a cyano group, or a nitrogen atom,

A denotes an imino group,

B denotes a carbonyl group,

C denotes a 1,2-vinylene or an ethynylene group,

D denotes a C_{1-4} -alkylene group,

A₂ a -CO-NR₄-alkylene group wherein the alkylene moiety contains 2 or 3 carbon atoms, while the linking to the adjacent group C must take place via the carbonyl group wherein

R_4 denotes a hydrogen atom,

or, if D is bound to a nitrogen atom of the group E, it may also denote a carbonyl group,

E denotes an R_6O-CO -alkylene-NR₅ or ($R_7O-PO-OR_8$)-alkylene-NR₅ group wherein in each case the alkylene moiety, which is straight-chained and contains 1 to 2 carbon atoms, may additionally be substituted by a methyl group or by an R_6O-CO or R_6O-CO -methyl group, while

R_5 denotes a hydrogen atom,

a C_{1-2} -alkyl group which may be substituted by an R_6O-CO group,

an ethyl group optionally substituted by one or two methyl groups, which is terminally substituted by a hydroxy, C_{1-2} -alkylcarbonylsulphenyl or C_{1-2} -alkylcarbonyloxy group,

a 2,2-dimethoxyethyl or 2,2-diethoxyethyl group,

R_6 denotes a hydrogen atom,

a C_{1-8} -alkyl group,

a cyclopentyl, cyclopentylmethyl, cyclohexyl or cyclohexylmethyl group,

a phenyl group optionally substituted by one or two methyl groups, a phenylmethyl group which may be substituted in the phenyl moiety by one or two methyl groups, a 5-indanyl group or an $R_g\text{CO-O-(R}_e\text{CR}_f)$ group, while

R_e denotes a hydrogen atom or a methyl group,

R_f denotes a hydrogen atom and

R_g denotes a C_{1-4} -alkyl or C_{1-2} -alkoxy group,

R_7 and R_8 , which may be identical or different, in each case denote a hydrogen atom, a methyl, ethyl or phenyl group,

a pyrrolidino or piperidino group which is substituted by an $R_6\text{O-CO}$ or $R_6\text{O-CO-methyl}$ group, wherein R_6 is as hereinbefore defined,

A² a pyrrolidino or piperidino group which is substituted by two $R_6\text{O-CO}$ or $R_6\text{O-CO-methyl}$ groups wherein R_6 is as hereinbefore defined,

a piperazino group which is substituted in the 4 position by the group R_{10} and additionally at a cyclic carbon atom by an $R_6\text{O-CO}$ group, while R_6 is as hereinbefore defined and

R_{10} denotes a hydrogen atom, a methyl or ethyl group,

a piperazino group which is substituted in the 4 position by an $R_6\text{O-CO-C}_{1-4}$ -alkyl, bis- $(R_6\text{O-CO})\text{-C}_{1-4}$ -alkyl or $(R_7\text{O-PO-OR}_8)\text{-C}_{1-2}$ -alkyl group wherein R_6 to R_8 are as hereinbefore defined,

a piperazino group which is substituted in the 4 position by an $R_6\text{O-CO-methyl}$ group and additionally at a cyclic carbon atom by an $R_6\text{O-CO}$ group wherein R_6 is as hereinbefore defined,

a morpholino group which is substituted by an $R_6\text{O-CO-}$ group, wherein R_6 is as hereinbefore defined,

a 2-oxo-morpholino group which may be substituted by 1 to 2 C_{1-2} -alkyl groups,

a 2-oxo-thiomorpholino group which may be substituted by 1 to 2 C_{1-2} -alkyl groups,

a morpholino group which is substituted in the 2 position by a methoxy or ethoxy group,

a morpholino group which is substituted in the 2 and 6 positions in each case by a methoxy or ethoxy group,

a 2,2-dimethoxyethyl-NR₅, 2,2-diethoxyethyl-NR₅ or 1,3-dioxolan-2-yl-methyl-NR₅-group wherein R₅ is as hereinbefore defined,

an N-methyl-R₁₁N or N-ethyl-R₁₁N group wherein

R₁₁ denotes a 2-oxo-tetrahydrofuran-3-yl or 2-oxo-tetrahydrofuran-4-yl group,

or D together with E denotes an R_gCO-O-(R_eCR_f)-O-CO group wherein R_e to R_g are as hereinbefore defined,

F and G together denote a hydrogen atom,

a methoxy, ethoxy, C₄₋₆-cycloalkoxy or C₃₋₆-cycloalkyl-C₁₋₃-alkoxy group,

the tautomers, the stereoisomers and the salts thereof.

Subgeneric aspect (9) of the invention is bicyclic heterocycles of general formula I, characterised in that R_b denotes one of the optionally substituted 1-phenyl-ethyl groups mentioned in the respective subgeneric aspects 5, 6, 7 or 8,

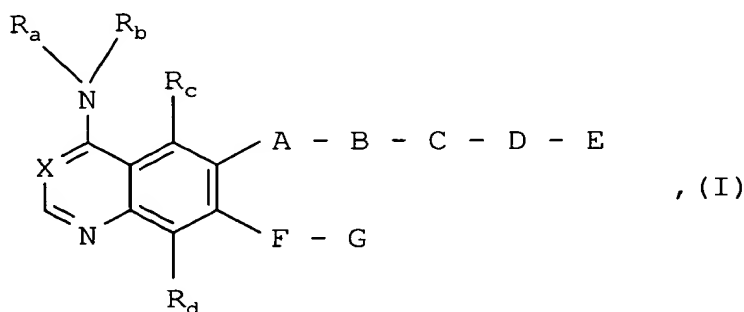
the tautomers, the stereoisomers and the salts thereof.

Subgeneric aspect (10) of the invention is bicyclic heterocycles of general formula I according to at least one of subgeneric aspects 5 to 8, characterised in that F and G together denote one of the cycloalkoxy or cycloalkyl-alkoxy groups mentioned in the respective subgeneric aspects 5, 6, 7 or 8,

the tautomers, the stereoisomers and the salts thereof.

Subgeneric aspect (11) of the invention is bicyclic heterocycles of general formula I according to at least one of subgeneric aspects 5 to 8, characterised in that E denotes one of the optionally substituted 2-oxo-morpholino groups mentioned in the respective subgeneric aspects 5, 6, 7 or 8.

Subgeneric aspect (12) of the invention is bicyclic heterocycles of general formula



wherein

R_a denotes a hydrogen atom or a C₁₋₄-alkyl group,

R_b denotes a phenyl, benzyl or 1-phenylethyl group wherein the phenyl nucleus is substituted in each case by the groups R₁ to R₃, whilst

R₁ and R₂, which may be identical or different, in each case denote a hydrogen, fluorine, chlorine, bromine or iodine atom,

a C₁₋₄-alkyl, hydroxy, C₁₋₄-alkoxy, C₃₋₆-cycloalkyl, C₄₋₆-cycloalkoxy, C₂₋₅-alkenyl or C₂₋₅-alkynyl group,

an aryl, aryloxy, arylmethyl or arylmethoxy group,

12 a C₃₋₅-alkenyloxy or C₃₋₅-alkynyloxy group, wherein the unsaturated moiety may not be linked to the oxygen atom,

a C₁₋₄-alkylsulphenyl, C₁₋₄-alkylsulphinyl, C₁₋₄-alkylsulphonyl, C₁₋₄-alkylsulphonyloxy, trifluoromethylsulphenyl, trifluoromethylsulphinyl or trifluoromethylsulphonyl group,

a methyl or methoxy group substituted by 1 to 3 fluorine atoms,

an ethyl or ethoxy group substituted by 1 to 5 fluorine atoms,

a cyano or nitro group or an amino group optionally substituted by one or two C₁₋₄-alkyl groups, wherein the substituents may be identical or different, or

R₁ together with R₂, if they are bound to adjacent carbon atoms, denote a -CH=CH-CH=CH-, -CH=CH-NH or -CH=N-NH group and

R₃ denotes a hydrogen, fluorine, chlorine or bromine atom,

a C₁₋₄-alkyl, trifluoromethyl or C₁₋₄-alkoxy group,

R_c and R_d, which may be identical or different, in each case denote a hydrogen, fluorine or chlorine atom, a methoxy group, or a methyl group optionally substituted by a methoxy, dimethylamino, diethylamino, pyrrolidino, piperidino or morpholino group,

X denotes a methine group substituted by a cyano group or a nitrogen atom,

A denotes an oxygen atom or an imino group optionally substituted by a C₁₋₄-alkyl group,

B denotes a carbonyl or sulphonyl group,

C denotes a 1,3-allenylene, 1,1 or 1,2-vinylene group which may be substituted in each case by one or two methyl groups or by a trifluoromethyl group,

an ethynylene group or

a 1,3-butadien-1,4-ylene group optionally substituted by 1 to 4 methyl groups or by a trifluoromethyl group,

A² D together with E denotes a hydrogen atom,

a C₁₋₄-alkyl group optionally substituted by 1 to 5 fluorine atoms,

a C₃₋₆-cycloalkyl group,

an aryl, heteroaryl, C₁₋₄-alkylcarbonyl, arylcarbonyl or C₁₋₄-alkoxycarbonyl group,

an aminocarbonyl, C₁₋₄-alkylaminocarbonyl or di-(C₁₋₄-alkyl)-aminocarbonyl group or

a carbonyl group, which is substituted by a 4- to 7-membered alkyleneimino group, whilst in the abovementioned 6- to 7-membered alkyleneimino groups, a methylene group in the 4 position may be replaced by an oxygen or sulphur atom, by an imino group substituted by the group R₁₀, by a sulphinyl or sulphonyl group, wherein R₁₀ is defined as in claim 1,

F denotes a C₁₋₆-alkylene group, a -O-C₁₋₆-alkylene group, wherein the alkylene moiety is linked to the group G, or an oxygen atom, whilst the latter may not be linked to a nitrogen atom of the group G, and

G denotes an R₆O-CO-alkylene-NR₅, (R₇O-PO-OR₈)-alkylene-NR₅ or (R₇O-PO-R₉)-alkylene-NR₅-group wherein in each case the alkylene moiety, which is straight-chained and contains 1 to 6 carbon atoms, may additionally be substituted by one or two C₁₋₂-alkyl groups or by an R₆O-CO or R₆O-CO-C₁₋₂-alkyl group, wherein R₅ to R₉ are defined as in claim 1,

a 4- to 7-membered alkyleneimino group which is substituted by an R₆O-CO, (R₇O-PO-OR₈), (R₇O-PO-R₉), R₆O-CO-C₁₋₄-alkyl, bis-(R₆O-CO)-C₁₋₄-alkyl, (R₇O-PO-OR₈)-C₁₋₄-alkyl or (R₇O-PO-R₉)-C₁₋₄-alkyl group wherein R₆ to R₉ are defined as in claim 1,

a 4- to 7-membered alkyleneimino group which is substituted by two R_6O-CO or $R_6O-CO-C_{1.4}$ -alkyl groups or by an R_6O-CO -group and an $R_6O-CO-C_{1.4}$ -alkyl group wherein R_6 is defined as in claim 1,

a piperazino or homopiperazino group which is substituted in the 4 position by the group R_{10} and is additionally substituted at a cyclic carbon atom by an R_6O-CO , $(R_7O-PO-OR_8)$, $(R_7O-PO-R_9)$, $R_6O-CO-C_{1.4}$ -alkyl, bis- $(R_6O-CO)-C_{1.4}$ -alkyl, $(R_7O-PO-OR_8)-C_{1.4}$ -alkyl or $(R_7O-PO-R_9)-C_{1.4}$ -alkyl group wherein R_6 to R_{10} are defined as in claim 1,

a piperazino or homopiperazino group which is substituted in the 4 position by the group R_{10} and is additionally substituted at cyclic carbon atoms by two R_6O-CO or $R_6O-CO-C_{1.4}$ -alkyl groups or by an R_6O-CO group and an $R_6O-CO-C_{1.4}$ -alkyl group wherein R_6 and R_{10} are defined as in claim 1,

A2 a piperazino or homopiperazino group which is substituted in each case in the 4 position by an $R_6O-CO-C_{1.4}$ -alkyl, bis- $(R_6O-CO)-C_{1.4}$ -alkyl, $(R_7O-PO-OR_8)-C_{1.4}$ -alkyl or $(R_7O-PO-R_9)-C_{1.4}$ -alkyl group wherein R_6 to R_9 are defined as in claim 1,

a piperazino or homopiperazino group which is substituted in the 4 position by an $R_6O-CO-C_{1.4}$ -alkyl, bis- $(R_6O-CO)-C_{1.4}$ -alkyl, $(R_7O-PO-OR_8)-C_{1.4}$ -alkyl or $(R_7O-PO-R_9)-C_{1.4}$ -alkyl group and is additionally substituted at cyclic carbon atoms by one or two R_6O-CO or $R_6O-CO-C_{1.4}$ -alkyl groups or by an R_6O-CO -group and an $R_6O-CO-C_{1.4}$ -alkyl group wherein R_6 to R_9 are defined as in claim 1,

a morpholino or homomorpholino group which is substituted in each case by an R_6O-CO , $(R_7O-PO-OR_8)$, $(R_7O-PO-R_9)$, $R_6O-CO-C_{1.4}$ -alkyl, bis- $(R_6O-CO)-C_{1.4}$ -alkyl, $(R_7O-PO-OR_8)-C_{1.4}$ -alkyl or $(R_7O-PO-R_9)-C_{1.4}$ -alkyl group wherein R_6 to R_9 are defined as in claim 1,

a morpholino or homomorpholino group which is substituted by two R_6O-CO or $R_6O-CO-C_{1.4}$ -alkyl groups or by an R_6O-CO -group and an $R_6O-CO-C_{1.4}$ -alkyl group wherein R_6 is defined as in claim 1,

a pyrrolidinyl, piperidinyl or hexahydroazepinyl group substituted in the 1 position by the group R_{10} , whilst the abovementioned 5- to 7-membered rings are in each case additionally substituted at a carbon atom by an R_6O-CO , $(R_7O-PO-OR_8)$, $(R_7O-PO-R_9)$, $R_6O-CO-C_{1.4}$ -alkyl, bis- $(R_6O-CO)-C_{1.4}$ -alkyl, $(R_7O-PO-OR_8)-C_{1.4}$ -alkyl or $(R_7O-PO-R_9)-C_{1.4}$ -alkyl group wherein R_6 to R_{10} are defined as in claim 1,

a pyrrolidinyl, piperidinyl or hexahydroazepinyl group substituted in the 1 position by the group R_{10} , while the abovementioned 5- to 7-membered rings are in each case additionally substituted at carbon atoms by two R_6O-CO or $R_6O-CO-C_{1.4}$ -alkyl groups or by an R_6O-CO -group and an $R_6O-CO-C_{1.4}$ -alkyl group wherein R_6 and R_{10} are defined as in claim 1,

a pyrrolidinyl, piperidinyl or hexahydroazepinyl group substituted in the 1 position by an $R_6O-CO-C_{1-4}$ -alkyl, bis- $(R_6O-CO)-C_{1-4}$ -alkyl, $(R_7O-PO-OR_8)-C_{1-4}$ -alkyl or $(R_7O-PO-R_9)-C_{1-4}$ -alkyl group wherein R_6 to R_9 are defined as in claim 1,

a pyrrolidinyl, piperidinyl or hexahydroazepinyl group substituted in the 1 position by an $R_6O-CO-C_{1-4}$ -alkyl, bis- $(R_6O-CO)-C_{1-4}$ -alkyl, $(R_7O-PO-OR_8)-C_{1-4}$ -alkyl or $(R_7O-PO-R_9)-C_{1-4}$ -alkyl group, while the abovementioned 5- to 7-membered rings are in each case additionally substituted at carbon atoms by one or two R_6O-CO or $R_6O-CO-C_{1-4}$ -alkyl groups or by an R_6O-CO -group and an $R_6O-CO-C_{1-4}$ -alkyl group wherein R_6 to R_9 are defined as in claim 1,

a 2-oxo-morpholino group which may be substituted by 1 or 2 methyl groups,

A² a 2-oxo-morpholinyl group which is substituted in the 4 position by a hydrogen atom, by a C_{1-4} -alkyl, $R_6O-CO-C_{1-4}$ -alkyl, $(R_7O-PO-OR_8)-C_{1-4}$ -alkyl or $(R_7O-PO-R_9)-C_{1-4}$ -alkyl group, while R_6 to R_9 are defined as in claim 1 and the abovementioned 2-oxo-morpholinyl groups are in each case linked to a carbon atom of the group F,

a morpholino or thiomorpholino group which is substituted in the 2 position by a C_{1-4} -alkoxy group,

a morpholino or thiomorpholino group which is substituted in the 2 and 6 position by a C_{1-4} -alkoxy group,

a C_{1-4} -alkyl- NR_5 -group wherein the C_{1-4} -alkyl moiety, which is straight-chained and may additionally be substituted by one or two methyl groups, is in each case terminally substituted by a di- $(C_{1-4}$ -alkoxy)-methyl or tri- $(C_{1-4}$ -alkoxy)-methyl group, whilst R_5 is defined as in claim 1,

a C_{1-4} -alkyl- NR_5 -group wherein the C_{1-4} -alkyl moiety, which is straight-chained and may additionally be substituted by one or two methyl groups, is terminally substituted in each case by a 1,3-dioxolan-2-yl or 1,3-dioxan-2-yl-group optionally substituted by one or two methyl groups, while R_5 is defined as in claim 1,

an R_hNR_5 -group wherein R_5 is as hereinbefore defined and R_h denotes a 2-oxo-tetrahydrofuran-3-yl, 2-oxo-tetrahydrofuran-4-yl, 2-oxo-tetrahydropyran-3-yl, 2-oxo-tetrahydropyran-4-yl or 2-oxo-tetrahydropyran-5-yl group optionally substituted by one or two methyl groups,

whilst by the aryl moieties mentioned in the definitions of the abovementioned groups is meant a phenyl group which in each case may be monosubstituted by R_{12} , mono-, di- or trisubstituted by R_{13} or monosubstituted by R_{12} and additionally mono- or disubstituted by R_{13} , whilst the substituents may be identical or different and

R_{12} denotes a cyano, carboxy, C_{1-4} -alkoxycarbonyl, aminocarbonyl, C_{1-4} -alkylaminocarbonyl, di- $(C_{1-4}$ -alkyl)-aminocarbonyl, C_{1-4} -alkylsulphenyl, C_{1-4} -alkylsulphinyl, C_{1-4} -alkylsulphonyl, hydroxy, C_{1-4} -alkylsulphonyloxy, trifluoromethoxy, nitro, amino, C_{1-4} -alkylamino, di- $(C_{1-4}$ -alkyl)-amino, C_{1-4} -alkyl-carbonylamino, N- $(C_{1-4}$ -alkyl)- C_{1-4} -alkylcarbonylamino, C_{1-4} -alkylsulphonylamino, N- $(C_{1-4}$ -alkyl)- C_{1-4} -alkylsulphonylamino, aminosulphonyl, C_{1-4} -alkylaminosulphonyl or di- $(C_{1-4}$ -alkyl)-aminosulphonyl group or a carbonyl group, which is substituted by a 5- to 7-membered alkyleneimino group, wherein in the abovementioned 6- to 7-membered alkyleneimino groups in each case a methylene group in the 4 position may be replaced by an oxygen or sulphur atom, by a sulphinyl, sulphonyl, imino or N- $(C_{1-4}$ -alkyl)-imino group, and

A^2 R_{13} denotes a fluorine, chlorine, bromine or iodine atom, a C_{1-4} -alkyl, trifluoromethyl or C_{1-4} -alkoxy group or

two groups R_{13} , if they are bound to adjacent carbon atoms, together denote a C_{3-5} -alkylene, methylenedioxy or 1,3-butadien-1,4-ylene group,

and moreover, the heteroaryl groups mentioned in the definitions of the abovementioned groups also include a 5-membered heteroaromatic group which contains an imino group, an oxygen or sulphur atom or an imino group, an oxygen or sulphur atom and one or two nitrogen atoms, or

a 6-membered heteroaromatic group which contains one, two or three nitrogen atoms,

whilst the abovementioned 5-membered heteroaromatic groups may be substituted in each case by 1 or 2 methyl or ethyl groups and the abovementioned 6-membered heteroaromatic groups may be substituted in each case by 1 or 2 methyl or ethyl groups or by a fluorine, chlorine, bromine or iodine atom, or by a trifluoromethyl, hydroxy, methoxy or ethoxy group,

the tautomers, the stereoisomers and the salts thereof.

Subgeneric aspect (13) of the invention comprises bicyclic heterocycles of general formula I according to subgeneric aspect 12, wherein

R_a denotes a hydrogen atom,

R_b denotes a phenyl, benzyl or 1-phenylethyl group wherein the phenyl nucleus is substituted in each case by the groups R_1 to R_3 , while

R_1 and R_2 , which may be identical or different, each denote a hydrogen, fluorine, chlorine, bromine or iodine atom,

a methyl, ethyl, hydroxy, methoxy, ethoxy, amino, cyano, vinyl or ethynyl group,

an aryl, aryloxy, arylmethyl or arylmethoxy group,

a methyl or methoxy group substituted by 1 to 3 fluorine atoms or

R₁ together with R₂, if they are bound to adjacent carbon atoms, denote a -CH=CH-CH=CH-, -CH=CH-NH or -CH=N-NH group and

R₃ denotes a hydrogen, fluorine, chlorine or bromine atom,

R_c and R_d in each case denote a hydrogen atom,

X denotes a methine group substituted by a cyano group or a nitrogen atom,

A denotes an imino group optionally substituted by a methyl or ethyl group,

B denotes a carbonyl group,

C denotes a 1,1- or 1,2-vinylene group which is substituted in each case by one or two methyl groups or may be substituted by a trifluoromethyl group,

an ethynylene group or

a 1,3-butadien-1,4-ylene group optionally substituted by a methyl or trifluoromethyl group,

D together with E denotes a hydrogen atom,

a methyl, trifluoromethyl or aryl group,

F denotes an -O-C₁₋₄-alkylene group, wherein the alkylene moiety is linked to the group G, or an oxygen atom, while this may not be linked to a nitrogen atom of the group G, and

G denotes an R₆O-CO-alkylene-NR₅, (R₇O-PO-OR₈)-alkylene-NR₅ or (R₇O-PO-R₉)-alkylene-NR₅ group wherein in each case the alkylene moiety, which is straight-chained and contains 1 to 4 carbon atoms, may additionally be substituted by one or two C₁₋₂-alkyl groups or by an R₆O-CO or R₆O-CO-C₁₋₂-alkyl group, while R₅ to R₉ are defined as in claim 2,

a 4- to 7-membered alkyleneimino group which is substituted by an R₆O-CO, R₆O-CO-C₁₋₄-alkyl or bis-(R₆O-CO)-C₁₋₄-alkyl group wherein R₆ is defined as in claim 2,

a 4- to 7-membered alkyleneimino group which is substituted by two R₆O-CO or R₆O-CO-C₁₋₄-alkyl groups wherein R₆ is defined as in claim 2,

a piperazino or homopiperazino group which is substituted in the 4 position by the group R_{10} and is additionally substituted at a cyclic carbon atom by an R_6O-CO , $R_6O-CO-C_{1-4}$ -alkyl or bis- $(R_6O-CO)-C_{1-4}$ -alkyl group wherein R_6 and R_{10} are defined as in claim 2,

a piperazino or homopiperazino group which is substituted in the 4 position by the group R_{10} and is additionally substituted at cyclic carbon atoms by two R_6O-CO or $R_6O-CO-C_{1-4}$ -alkyl groups wherein R_6 and R_{10} are defined as in claim 2,

a piperazino or homopiperazino group which is substituted in each case in the 4 position by an $R_6O-CO-C_{1-4}$ -alkyl, bis- $(R_6O-CO)-C_{1-4}$ -alkyl, $(R_7O-PO-OR_8)-C_{1-4}$ -alkyl or $(R_7O-PO-R_9)-C_{1-4}$ -alkyl group wherein R_6 to R_9 are defined as in claim 2,

A²
a piperazino or homopiperazino group which is substituted in the 4 position by an $R_6O-CO-C_{1-4}$ -alkyl or bis- $(R_6O-CO)-C_{1-4}$ -alkyl group and additionally at cyclic carbon atoms by one or two R_6O-CO or $R_6O-CO-C_{1-4}$ -alkyl groups wherein R_6 is defined as in claim 2,

a morpholino or homomorpholino group which is substituted in each case by an R_6O-CO , $R_6O-CO-C_{1-4}$ -alkyl or bis- $(R_6O-CO)-C_{1-4}$ -alkyl group wherein R_6 is defined as in claim 2,

a morpholino or homomorpholino group which is substituted by two R_6O-CO or $R_6O-CO-C_{1-4}$ -alkyl groups wherein R_6 is defined as in claim 2,

a pyrrolidinyl, piperidinyl or hexahydroazepinyl group substituted in the 1 position by the group R_{10} , while the abovementioned 5- to 7-membered rings in each case are additionally substituted at a carbon atom by an R_6O-CO , $R_6O-CO-C_{1-4}$ -alkyl or bis- $(R_6O-CO)-C_{1-4}$ -alkyl group wherein R_6 and R_{10} are defined as in claim 2,

a pyrrolidinyl, piperidinyl or hexahydroazepinyl group substituted in the 1 position by the group R_{10} , while the abovementioned 5- to 7-membered rings in each case are additionally substituted at carbon atoms by two R_6O-CO or $R_6O-CO-C_{1-4}$ -alkyl groups wherein R_6 and R_{10} are defined as in claim 2,

a pyrrolidinyl, piperidinyl or hexahydroazepinyl group substituted in the 1 position by an $R_6O-CO-C_{1-4}$ -alkyl, bis- $(R_6O-CO)-C_{1-4}$ -alkyl, $(R_7O-PO-OR_8)-C_{1-4}$ -alkyl or $(R_7O-PO-R_9)-C_{1-4}$ -alkyl group wherein R_6 to R_9 are defined as in claim 2,

a pyrrolidinyl, piperidinyl or hexahydroazepinyl group substituted in the 1 position by an $R_6O-CO-C_{1-4}$ -alkyl or bis- $(R_6O-CO)-C_{1-4}$ -alkyl group, while the abovementioned 5- to 7-membered rings in each case are additionally substituted at carbon atoms by one or two R_6O-CO or $R_6O-CO-C_{1-4}$ -alkyl groups wherein R_6 is defined as in claim 2,

a 2-oxo-morpholino group which may be substituted by 1 or 2 methyl groups,

a 2-oxo-morpholinyl group which is substituted in the 4 position by a C₁₋₄-alkyl or R₆O-CO-C₁₋₄-alkyl group, while R₆ is defined as in claim 2 and the abovementioned 2-oxo-morpholinyl groups are each are linked to a carbon atom of the group F,

a morpholino group which is substituted in the 2 position by a C₁₋₄-alkoxy group,

a morpholino group which is substituted in the 2 and 6 positions in each case by a C₁₋₄-alkoxy group,

a C₁₋₄-alkyl-NR₅ group wherein the C₁₋₄-alkyl moiety, which is straight-chained, is terminally substituted by a di-(C₁₋₄-alkoxy)-methyl group, while R₅ is defined as in claim 2,

A²
a C₁₋₄-alkyl-NR₅ group wherein the C₁₋₄-alkyl moiety, which is straight-chained, is terminally substituted by a 1,3-dioxolan-2-yl or 1,3-dioxan-2-yl group, while R₅ is defined as in claim 2,

a R_hNR₅ group wherein R₅ is defined as in claim 2 and R_h denotes a substituted 2-oxo-tetrahydrofuran-3-yl, 2-oxo-tetrahydrofuran-4-yl, 2-oxo-tetrahydropyran-3-yl, 2-oxo-tetrahydropyran-4-yl or 2-oxo-tetrahydropyran-5-yl group optionally by one or two methyl groups,

while the aryl moieties mentioned in the definition of the abovementioned groups denote a phenyl group which may in each case be monosubstituted by R₁₂, mono- or disubstituted by R₁₃ or monosubstituted by R₁₂ and additionally mono or disubstituted by R₁₃, while the substituents may be identical or different and

R₁₂ denotes a cyano, C₁₋₂-alkoxycarbonyl, aminocarbonyl, C₁₋₂-alkylaminocarbonyl, di-(C₁₋₂-alkyl)-aminocarbonyl, C₁₋₂-alkylsulphenyl, C₁₋₂-alkylsulphinyl, C₁₋₂-alkylsulphonyl, hydroxy, nitro, amino, C₁₋₂-alkylamino or di-(C₁₋₂-alkyl)-amino group and

R₁₃ denotes a fluorine, chlorine, bromine or iodine atom, a C₁₋₂-alkyl, trifluoromethyl or C₁₋₂-alkoxy group or

two groups R₁₃, if they are bound to adjacent carbon atoms, together denote a C₃₋₅-alkylene, methylenedioxy or 1,3-butadien-1,4-ylene group,

the tautomers, the stereoisomers and the salts thereof.

Subgeneric aspect (14) of the invention comprises bicyclic heterocycles of general formula I according to subgeneric aspect 12, wherein

R_a denotes a hydrogen atom,

R_b denotes a phenyl, benzyl or 1-phenylethyl group wherein the phenyl nucleus is substituted in each case by the groups R_1 to R_3 , while

R_1 and R_2 , which may be identical or different, each denote a hydrogen, fluorine, chlorine or bromine atom, or a methyl, trifluoromethyl, methoxy, ethynyl or cyano group,

R_3 denotes a hydrogen atom,

R_c and R_d in each case denote a hydrogen atom,

X denotes a methine group substituted by a cyano group, or a nitrogen atom,

A denotes an imino group,

B denotes a carbonyl group,

C denotes a 1,1- or 1,2-vinylene group,

an ethynylene group or

a 1,3-butadien-1,4-ylene group,

D together with E denotes a hydrogen atom,

a methyl, trifluoromethyl or aryl group,

F denotes an $-O-C_{1-4}$ -alkylene group, wherein the alkylene moiety is linked to the group G , or an oxygen atom, while this may not be linked to a nitrogen atom of the group G , and

G denotes an R_6O-CO -alkylene- NR_5 group wherein the alkylene moiety, which is straight-chained and contains 1 to 4 carbon atoms, may additionally be substituted by one or two C_{1-2} -alkyl groups or by an R_6O-CO or $R_6O-CO-C_{1-2}$ -alkyl group, while R_5 and R_6 are defined as in claim 3,

a pyrrolidino or piperidino group which is substituted by an R_6O-CO or $R_6O-CO-C_{1-2}$ -alkyl group wherein R_6 is defined as in claim 3,

a pyrrolidino or piperidino group which is substituted by two R_6O-CO or $R_6O-CO-C_{1-2}$ -alkyl groups wherein R_6 is defined as in claim 3,

a piperazino group which is substituted in the 4 position by the group R_{10} and additionally at a cyclic carbon atom by an R_6O-CO , or $R_6O-CO-C_{1-2}$ -alkyl group, while R_6 and R_{10} are defined as in claim 3,

a piperazino group which is substituted in the 4 position by an $R_6O-CO-C_{1-4}$ -alkyl, bis- $(R_6O-CO)-C_{1-4}$ -alkyl or $(R_7O-PO-OR_8)-C_{1-2}$ -alkyl group wherein R_6 to R_8 are defined as in claim 3,

a piperazino group which is substituted in the 4 position by an $R_6O-CO-C_{1-2}$ -alkyl group and additionally at a cyclic carbon atom by an R_6O-CO or $R_6O-CO-C_{1-2}$ -alkyl group wherein R_6 is defined as in claim 3,

a morpholino group which is substituted by an R_6O-CO or $R_6O-CO-C_{1-2}$ -alkyl group, while R_6 is defined as in claim 3,

a piperidinyl group substituted in the 1 position by an $R_6O-CO-C_{1-4}$ -alkyl, bis- $(R_6O-CO)-C_{1-4}$ -alkyl or $(R_7O-PO-OR_8)-C_{1-2}$ -alkyl group wherein R_6 to R_8 are defined as in claim 3,

A2
a 2-oxo-morpholino group which may be substituted by 1 or 2 methyl groups,

a 2-oxo-morpholinyl group which is substituted in the 4 position by a methyl, ethyl or $R_6O-CO-C_{1-2}$ -alkyl group, while R_6 is defined as in claim 3 and the abovementioned 2-oxo-morpholinyl groups in each case are linked to a carbon atom of the group F,

a morpholino group which is substituted in the 2 position by a methoxy or ethoxy group,

a morpholino group which is substituted in the 2 and 6 positions in each case by a methoxy or ethoxy group,

a 2,2-dimethoxyethyl- NR_5 , 2,2-diethoxyethyl- NR_5 , 1,3-dioxolan-2-yl-methyl- NR_5 or 1,3-dioxan-2-yl-methyl- NR_5 group wherein R_5 is defined as in claim 3,

while the aryl moieties mentioned in the definition of the abovementioned groups denote a phenyl group which may be mono- or disubstituted by R_{13} , while the substituents may be identical or different and

R_{13} denotes a fluorine, chlorine, bromine or iodine atom, a C_{1-2} -alkyl, trifluoromethyl or C_{1-2} -alkoxy group or

two groups R_{13} , if they are bound to adjacent carbon atoms, together denote a C_{3-4} -alkylene, methylenedioxy or 1,3-butadien-1,4-ylene group,

the tautomers, the stereoisomers and the salts thereof.

Subgeneric aspect (15) of the invention comprises bicyclic heterocycles of general formula I according to subgeneric aspect 12, wherein

denotes a hydrogen atom,

R_b denotes a phenyl, benzyl or 1-phenylethyl group wherein the phenyl nucleus is substituted in each case by the groups R_1 to R_3 , wherein

R_1 and R_2 , which may be identical or different, each denote a hydrogen, fluorine, chlorine or bromine atom or a methyl group and

R_3 denotes a hydrogen atom,

R_c and R_d each denote a hydrogen atom,

X denotes a methine group substituted by a cyano group, or a nitrogen atom,

A denotes an imino group,

B denotes a carbonyl group,

C denotes a 1,2-vinylene or an ethynylene group,

D together with E denotes a hydrogen atom or a methyl group,

F denotes an $-O-C_{1-4}$ -alkylene group, while the alkylene moiety is linked to the group G, or an oxygen atom, which may not be linked to a nitrogen atom of the group G, and

G denotes an R_6O-CO -alkylene- NR_5 group wherein the alkylene moiety, which is straight-chained and contains 1 or 2 carbon atoms, may additionally be substituted by a methyl group or by an R_6O-CO or R_6O-CO -methyl group, while R_5 and R_6 are defined as in claim 4,

a pyrrolidino or piperidino group which is substituted by an R_6O-CO or R_6O-CO -methyl group wherein R_6 is defined as in claim 4,

a pyrrolidino or piperidino group which is substituted by two R_6O-CO or R_6O-CO -methyl groups wherein R_6 is defined as in claim 4,

a piperazino group which is substituted in the 4 position by an $R_6O-CO-C_{1-4}$ -alkyl, bis- $(R_6O-CO)-C_{1-4}$ -alkyl or $(R_7O-PO-OR_8)-C_{1-2}$ -alkyl group wherein R_6 to R_8 are defined as in claim 4,

a piperidinyl group substituted in the 1 position by an $R_6O-CO-C_{1-2}$ -alkyl group wherein R_6 is defined as in claim 4,

the tautomers, the stereoisomers and the salts thereof.

Subgeneric aspect (16) of the invention comprises bicyclic heterocycles of general formula I according to at least one of subgeneric aspects 12 to 15, characterised in that R_b denotes one of the optionally substituted 1-phenyl-ethyl groups mentioned in the respective subgeneric aspects 12, 13, 14 or 15,

the tautomers, the stereoisomers and the salts thereof.

Subgeneric aspect (17) of the invention is the following compounds of general formula I:

- A²
- (a) 4-[(3-bromophenyl)amino]-7-(3-{4-[(ethoxycarbonyl)methyl]-piperazin-1-yl}propyloxy)-6-[(vinylcarbonyl)amino]-quinazoline,
- (b) 4-[(3-bromophenyl)amino]-7-(3-{4-[3-(ethoxycarbonyl)propyl]-piperazin-1-yl}propyloxy)-6-[(vinylcarbonyl)amino]-quinazoline,
- (c) 4-[(3-bromophenyl)amino]-7-({1-[(ethoxycarbonyl)methyl]-piperidin-4-yl}oxy)-6-[(vinylcarbonyl)amino]-quinazoline,
- (d) 4-[(3-bromophenyl)amino]-7-(3-{4-[(diethoxyphosphoryl)methyl]-piperazin-1-yl}propyloxy)-6-[(vinylcarbonyl)amino]-quinazoline,
- (e) 4-[(3-bromophenyl)amino]-7-(3-{N-[(ethoxycarbonyl)methyl]-N-methylamino}propyloxy)-6-[(vinylcarbonyl)amino]-quinazoline,
- (f) 4-[(3-bromophenyl)amino]-6-[(4-{N-[(ethoxycarbonyl)methyl]-N-methylamino}-1-oxo-2-buten-1-yl)amino]-quinazoline,
- (g) 4-[(3-bromophenyl)amino]-6-[(4-{N-[(diethoxyphosphoryl)methyl]-N-methylamino}-1-oxo-2-buten-1-yl)amino]-7-methoxy-quinazoline,
- (h) (R)-4-[(1-phenylethyl)amino]-6-[(4-{N-[(ethoxycarbonyl)methyl]-N-methylamino}-1-oxo-2-buten-1-yl)amino]-7-methoxy-quinazoline,
- (i) 4-[(3-bromophenyl)amino]-6-({4-[N-(2,2-dimethoxyethyl)-N-methylamino]-1-oxo-2-buten-1-yl}amino)-7-methoxy-quinazoline,
- (j) 4-[(3-bromophenyl)amino]-6-{[4-(2-ethoxy-morpholin-4-yl)-1-oxo-2-buten-1-yl]amino}-7-methoxy-quinazoline,
- (k) 4-[(3-bromophenyl)amino]-3-cyano-6-[(4-{N-[(ethoxycarbonyl)methyl]-N-methylamino}-1-oxo-2-buten-1-yl)amino]-quinoline,
- (l) 4-[(3-chloro-4-fluorophenyl)amino]-6-[(4-{4-[(ethoxycarbonyl)methyl]-piperazin-1-yl}-1-oxo-2-buten-1-yl)amino]-7-cyclopropylmethoxy-quinazoline,
- (m) 4-[(3-chloro-4-fluorophenyl)amino]-6-[(4-{N-[2-(ethoxycarbonyl)-ethyl]-N-[(ethoxycarbonyl)methyl]amino}-1-oxo-2-buten-1-yl)amino]-7-cyclopropylmethoxy-quinazoline,
- (n) 4-[(3-chloro-4-fluorophenyl)amino]-6-{[4-(2-oxo-morpholin-4-yl)-1-oxo-2-buten-1-yl]amino}-7-cyclopropylmethoxy-quinazoline,

(o) 4-[(3-chloro-4-fluorophenyl)amino]-6-[(4-{4-[(ethoxycarbonyl)methyl]-piperazin-1-yl}-1-oxo-2-buten-1-yl)amino]-7-cyclobutyloxy-quinazoline,

(p) 4-[(3-chloro-4-fluorophenyl)amino]-6-[(4-{4-[(ethoxycarbonyl)methyl]-piperazin-1-yl}-1-oxo-2-buten-1-yl)amino]-7-(2-cyclopropylethoxy)-quinazoline,

A²
(q) (S)-4-[(3-chloro-4-fluorophenyl)amino]-6-({4-[2-(methoxycarbonyl)-pyrrolidin-1-yl]-1-oxo-2-buten-1-yl}amino)-7-cyclopropylmethoxy-quinazoline,

(r) 4-[(3-chloro-4-fluorophenyl)amino]-6-[(4-{N-[(ethoxycarbonyl)methyl]-N-[2-(acetylsulphanyl)ethyl]amino}-1-oxo-2-buten-1-yl)amino]-7-cyclopropylmethoxy-quinazoline und

(s) 4-[(3-chloro-4-fluorophenyl)amino]-6-[(4-{N-[(ethoxycarbonyl)-methyl]-N-[2-(methylcarbonyloxy)ethyl]amino}-1-oxo-2-buten-1-yl)amino]-7-cyclopropylmethoxy-quinazoline

and the salts thereof.
